STIC-ILL

From: Canella, Karen
Sent: Thursday, October 16, 2003 8:39 PM
To: STIC-ILL
Subject: ill order 09/825,012

Art Unit 1642 Location 8E12(mail)

Telephone Number 308-8362

Application Number 09/825,012

1. Therapeutic Immunology, 1994, Vol. 1, No. 2, pp. 83-93

2. Cancer research:
   1996 Nov 15, 56(22):5179-5185
   1995 Mar 1, 55(5):1060-1069

3. Cancer Immunology, Immunotherapy, 1997 Aug, 44(6):323-328

4. American Environmental Laboratory, 1996 8(9):22-23

5. Modern Pathology, 1992 Nov, 5(6):603-606

6. Proceedings of the American Association for Cancer Research Annual Meeting, Mar 2000, Vol. 41, page 289

7. Annals of the New York Academy of Sciences, 1986, Vol. 464, pp. 389-399

(FILE 'HOME' ENTERED AT 18:16:37 ON 16 OCT 2003)

FILE 'MEDLINE, BIOSIS, SCISEARCH, CANCERLIT, LIFESCI, BIOTECHDS, CAPLUS'
ENTERED AT 18:16:59 ON 16 OCT 2003

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L1          4427 S HMFG# OR (MILK(W)FAT(W)GLOBULE)
L2          7104 S MFG
L3         11421 S L1 OR L2
L4             8 S L3 AND INTERNALI?
L5             5 DUP REM L4 (3 DUPLICATES REMOVED)
L6         19535 S PEM# OR (POLYMORPHIC(W)EPITHELIAL(W)MUCIN#) OR MUC OR MUC1 OR
L7         30507 S L3 OR L6
L8           449 S L3 AND L6
L9            83 S L8 AND (FUSION# OR FUSED OR CHIMERIC OR CHIMERA OR CONJUGAT#
L10           61 S L9 AND PY<2001
L11            5 S L8 AND IMMUNOTOXIN#
L12            4 S L11 AND PY<2001
L13           63 S L10 OR L12
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L17          235 S L7 AND (RICIN# OR GELONIN# OR RNASE# OR DNASE# OR RIBONUCLEA
L18           22 S L7 AND (RICIN# OR GELONIN#)
L19          219 S L7 AND (RNASE# OR DNASE# OR RIBONUCLEASE# OR DEOXYRIBONUCLEA
L20           30 S L19 AND (FUSION OR FUSED OR CONJUGATE OR CONJUGATED OR CHIME
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L22           29 S L21 AND PY<2001
L23           14 DUP REM L22 (15 DUPLICATES REMOVED)
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L25          258 S L24 AND IMMUNOTOXIN#
L26            2 S L25 AND (NUCLEAR)
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L29           23 S L24(5A)(NUCLEAR(3A)TARGET?)
L30           17 S L29 AND PY<2001
L31            8 DUP REM L30 (9 DUPLICATES REMOVED)
L32            0 S L24(S)(NUCLEAR(W)SIGNAL(W)SEQUENCE)
L33            0 S L24 AND (NUCLEAR(W)SIGNAL(W)SEQUENCE)
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L35         2546 S L24(3A)NUCLEAR
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L37            3 S L24(5A)(NUCLEAR(3A)TRANSPORT?)
L38           82 S L24(S)(NUCLEAR(3A)TRANSPORT?)
L39           10 S L24(5A)(NUCLEAR(3A)IMPORT?)
L40            5 S L39 AND PY<2001
L41            4 DUP REM L40 (1 DUPLICATE REMOVED)
L42           55 S L24 AND (NUCLEAR(3A)(IMPORT OR IMPORTING OR IMPORTATION))
L43           35 S L42 AND PY<2001
L44           20 DUP REM L43 (15 DUPLICATES REMOVED)
L45           46 S L24(5A)(SIGNAL(W)SEQUENCE)
L46            3 S L45 AND (NUCLEAR OR NUCLEASE)
L47            1 S L45 AND NUCLEUS
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FILE 'PCTFULL, USPATFULL, EUROPATFULL' ENTERED AT 19:37:41 ON 16 OCT 2003

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L49          500 S L48(5A)(NUCLEAR OR NUCLEUS)
L50           19 S L49(5A)(TARGET? OR IMPORT OR IMPORTATION OR TRANSPORT?)
L51        19103 S HMFG# OR (MILK(W)FAT(W)GLOBULE) OR MFG OR PEM# OR (POLYMORPHI
L52          128 S L48(S)L51
L53          212 S ANTI(2W)L51
L54          397 S L51(3A)(ANTIBOD? OR IMMUNOGLOBULIN# OR (BINDING(W)PARTNER#))
L55          439 S L53 OR L54
L56            3 S L55(S)(DNASE# OR HUMDNASE# OR HUMDNASE# OR HUMANDNASE# OR DE
L57           13 S L55(S)(RNASE# OR HRNASE# OR HUMRNASE# OR HUMANRNASE# OR RIBO
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L58 16 S L51(5A)(IMMUNOTOXIN# OR GELONIN# OR RICIN# OR ENDOTOXIN# OR

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:407220 CAPLUS
DOCUMENT NUMBER: 119:7220
TITLE: Humanized antibodies to human milk fat globules
INVENTOR(S): Adair, John Robert; Hamann, Philip R.; Owens, Raymond John; Baker, Terence Seward; Lyons, Alan Howard; Hinman, Lois M.; Menendez, Ana T.
PATENT ASSIGNEE(S): Celltech Ltd., UK
SOURCE: Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 534742	A1	19930331	EP 1992-308680	19920924
EP 534742	B1	19971119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2095926	AA	19930327	CA 1992-2095926	19920924
CA 2095926	C	20020716		
WO 9306231	A1	19930401	WO 1992-GB1759	19920924
W: AU, CA, CS, FI, HU, JP, KR, NO				
AU 9225983	A1	19930427	AU 1992-25983	19920924
AU 666868	B2	19960229		
EP 781845	A2	19970702	EP 1997-200482	19920924
EP 781845	A3	19970709		
EP 781845	B1	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 160362	E	19971215	AT 1992-308680	19920924
ES 2108732	T3	19980101	ES 1992-308680	19920924
IL 103269	A1	19980104	IL 1992-103269	19920924
AT 236251	E	20030415	AT 1997-200482	19920924
US 6506881	B1	20030114	US 1995-450809	19950525

PRIORITY APPLN. INFO.:
GB 1991-20467 A 19910926
US 1992-948541 A1 19920922
EP 1992-308680 A3 19920924
WO 1992-GB1759 A 19920924

AB Chimeric and complementarity-detg. region (CDR)-grafted humanized antibodies to human milk fat globules are prepd. for use in the diagnosis and treatment of breast cancer. The CDRs are derived from the mouse IgG1.kappa. monoclonal antibody CTMO1 that recognizes an antigen found in high levels in blood of breast cancer patients. The antibody may be conjugated with antitumor agents for treatment of the disease. The genes for the humanized antibodies were constructed by std. methods and expressed in CHO-L761 cells. Binding and **internalization** of the humanized antibodies by breast carcinoma cell lines was demonstrated. Conjugation of the antibodies with calicheamicin .gamma.1I was demonstrated.

L19 ANSWER 2 OF 15 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 97069874 MEDLINE
DOCUMENT NUMBER: 97069874 PubMed ID: 8912854
TITLE: Biodistribution of (111)indium-labeled engineered human antibody CTMO1 in ovarian cancer patients: influence of protein dose.
AUTHOR: van Hof A C; Molthoff C F; Davies Q; Perkins A C; Verheijen R H; Kenemans P; den Hollander W; Wilhelm A J; Baker T S; Sopwith M; Frier M; Symonds E M; Roos J C
CORPORATE SOURCE: Department of Obstetrics and Gynecology, University Hospital Vrije Universiteit, Amsterdam, the Netherlands.
SOURCE: CANCER RESEARCH, **(1996 Nov 15)** 56 (22) 5179-85.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970107

AB Thirty-one patients suspected of having ovarian cancer received a single i.v. injection of radiolabeled (100 MBq (111)In) engineered human CTMO1 (hCTMO1) to investigate its potential as an **internalizing** drug carrier. hCTMO1 is a complementary-determining region-grafted human IgG4 monoclonal antibody recognizing an ovarian carcinoma-associated antigen, the **MUC**-1-gene product. The amount of radioactivity was determined in tumor tissue, various normal tissues, including liver biopsies, and blood samples obtained at laparotomy, 6 days after injection of either 0.1 or 1.0 mg hCTMO1/kg of body weight. Circulating antigen-15-3 was measurable in all patients before injection, and immune complex formation was already present at the end of infusion. In the 0.1 mg/kg group, most of the radioactivity was bound to immune complexes, whereas in the 1.0 mg/kg group, most was bound to IgG monomers. Increasing the hCTMO1 dose 10-fold did not influence the overall disappearance of (111)In from the blood, but the elimination half-life of (111)indium bound to immune complexes was increased 2-fold. Uptake in tumor tissue 6 days postinjection at the 0.1 mg/kg dose was 7.6 times higher (P = 0.0009) than in normal tissue and 2.5 times higher (P = 0.03) than in blood. At the 1.0 mg/kg dose, the uptake in tumor tissue was 14.0 times higher (P = 0.0003) than in normal tissue and 8.1 times higher (P = 0.0007) than in blood. Liver activity was substantial (23.7 +/- 10.5 and 18.3 +/- 6.7% of the injected dose/kg for the 0.1 and 1.0 mg/kg dose group, respectively). These results are superior to those found with other clinically tested anti-**MUC**-1 gene product antibodies. hCTMO1 seems to be a suitable carrier for cytotoxic agents in ovarian carcinoma patients; the better uptake results and tumor-to-blood ratios are obtained at the higher dose of 1.0 mg hCTMO1/kg body weight.

L19 ANSWER 1 OF 15 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 97442385 MEDLINE
DOCUMENT NUMBER: 97442385 PubMed ID: 9298934
TITLE: Comparison of the biological properties of two anti-mucin-1 antibodies prepared for imaging and therapy.
AUTHOR: Pietersz G A; Wenjun L; Krauer K; Baker T; Wreschner D; McKenzie I F
CORPORATE SOURCE: Austin Research Institute, Heidelberg, Victoria, Australia.
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, **(1997 Aug)** 44 (6) 323-8.
Journal code: 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971021
Last Updated on STN: 19971021
Entered Medline: 19971006

AB A comparison was made between the murine anti-**MUC1** antibody BC2 (which reacts with the peptide epitope APDTR) and the "humanised" antibody hCTMO1 from CellTech, which reacts with the **MUC1** epitope RPAP. Preliminary studies demonstrated that hCTMO1 was a "good" antibody whereas BC2 was not. Various parameters were determined and conclusions reached. (a) Affinity: the affinity of hCTMO1 was 2.60 x 10(7) M(-1) and that of BC2 was 1.36 x 10(7) M(-1); we did not consider these numbers to be substantially different, although hCTMO1 was clearly of higher affinity than BC2. (b) On/off rate at 4 degrees C: both antibodies bound effectively to the **MUC**-1 transfectant MOR5-CF2; the association rate for hCTMO1 was 3.8 times that of BC2 and the dissociation rate for BC2 was twice as fast as that of hCTMO1. (c) On/off rates at 37 degrees C: at 37 degrees C the association rate for hCTMO1 was greater than that of BC2. (d) **Internalization**: hCTMO1 was also more efficient at internalising bound antibody; 70% of bound hCTMO1 was internalised, whilst 6% of bound BC2 was internalised. From these studies it was clear that, while hCTMO1 was of similar affinity to BC2, the faster uptake and internalisation and lower off rate indicated that it was likely to be a superior antibody; this was proven in vivo. (e) Localisation: hCTMO1 bound much better in vivo than BC2 (68% compared to 28%). (f) Therapeutic experiments: BC2-idarubicin conjugates were essentially ineffective in eradicating tumours in mice whereas hCTMO1-idarubicin had a dramatic effect on breast cancer tumour cells growing in mice. We conclude that the simple measurements on/off rates and internalisation at 37 degrees C are the most important parameters to use to determine antibody effectiveness, prior to embarking on clinical studies.

L19 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:813719 CAPLUS
Correction of: 1996:720365
DOCUMENT NUMBER: 135:322637
Correction of: 126:11318
TITLE: Biodistribution of 111Indium-labeled engineered human antibody CTM01 in ovarian cancer patients: influence of protein dose
AUTHOR(S): van Hout, Piet; Pipkin, William
CORPORATE SOURCE: Hewlett-Packard GmbH, Waldbronn, Germany
SOURCE: American Environmental Laboratory (**1996**), 8(9), 22-23
CODEN: AELAEL; ISSN: 1051-2306
PUBLISHER: International Scientific Communications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thirty-one patients suspected of having ovarian cancer received a single i.v. injection of radiolabeled (100 MBq 111In) engineered human CTM01 (hCTM01) to investigate its potential as an **internalizing** drug carrier. HCTM01 is a complementary-detg. region-grafted human IgG4 monoclonal antibody recognizing an ovarian carcinoma-assocd. antigen, the **MUC**-1-gene product. The amt. of radioactivity was detd. in tumor tissue, various normal tissues, including liver biopsies, and blood samples obtained at laparotomy, 6 days after injection of either 0.1 or 1.0 mg hCTM01/kg of body wt. Circulating antigen-15-3 was measurable in all patients before injection, and immune complex formation was already present at the end of infusion. In the 0.1 mg/kg group, most of the radioactivity was bound to immune complexes, whereas in the 1.0 mg/kg group, most was bound to IgG monomers. Increasing the hCTM01 dose 10-fold did not influence the overall disappearance of 111In from the blood, but he elimination half-life of 111indium bound to immune complexes was increased 2-fold. Uptake in tumor tissue 6 days postinjection at the 0.1 mg/kg dose was 7.6 times higher than in normal tissue and 2.5 times higher than in blood. At the 1.0 mg/kg dose, the uptake in tumor tissue was 14.0 times higher than in normal tissue and 8.1 times higher than in blood. Liver activity was substantial (23.7.+-.10.5 and 18.3.+-.6.7% of the injected dose/kg for the 0.1 and 1.0 mg/kg dose group, resp.). These results are superior to those found with other clin. tested anti-**MUC**-1 gene product antibodies. HCTM01 seems to be a suitable carrier for cytotoxic agents in ovarian carcinoma patients; the better uptake results and tumor-to-blood ratios are obtained at the higher dose of 1.0 mg hCTM01/kg body wt.

L5 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 95357344 MEDLINE
DOCUMENT NUMBER: 95357344 PubMed ID: 1369793
TITLE: Subcellular localization of **HMFG2** in breast carcinomas: an immunohistochemical and immunoelectron microscopic study.
AUTHOR: Hanna W M; Kahn H J; Zive S E; Shackleton M; Andrighetti L
CORPORATE SOURCE: Department of Pathology, Women's College Hospital, University of Toronto, Ontario, Canada.
SOURCE: MODERN PATHOLOGY, (1992 Nov) 5 (6) 603-6.
Journal code: 8806605. ISSN: 0893-3952.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950921
Last Updated on STN: 19970203
Entered Medline: 19950907

AB Malignant transformation of human cells is associated with morphological and biochemical alterations. We have studied the distribution and pattern of staining of **HMFG2** (human milk fat globulin) in normal breast, benign breast lesions, and 137 primary and metastatic breast carcinomas. Immunohistochemical staining was performed with an antibody to **HMFG2** using the indirect peroxidase technique. Three patterns of staining were noted: 1) secretion and luminal staining (in normal breast, most benign breast lesions and some breast carcinomas); 2) plasma membrane staining (in breast carcinomas); 3) intracytoplasmic staining (in breast carcinomas). Immunoelectron microscopy was also performed on normal breast, infiltrating duct, and lobular carcinomas. Immunoelectron microscopy showed localization of the gold particles on the electron dense granules of the **HMFG2** protein. These were localized along the surface of the extracytoplasmic lumina in normal breast ducts/acini and breast carcinomas, whereas localization was also noted within the intracytoplasmic lumina in cancer cells only. These results show that there is altered localization of milk fat globulin in breast cancer cells associated with membrane **internalization** and formation of intracytoplasmic lumina. This contributes to the understanding of the phenotypic alterations associated with malignant transformation in breast cancer.

L13 ANSWER 42 OF 63 CANCERLIT on STN
ACCESSION NUMBER: 95171371 CANCERLIT
DOCUMENT NUMBER: 95171371 PubMed ID: 7866989
TITLE: Pharmacokinetics, biodistribution, and dosimetry of specific and control radiolabeled monoclonal antibodies in patients with primary head and neck squamous cell carcinoma.
AUTHOR: Maraveyas A; Stafford N; Rowlinson-Busza G; Stewart J S; Epenetos A A
CORPORATE SOURCE: Department of Clinical Oncology, Royal Postgraduate Medical School, Hammersmith Hospital, London, United Kingdom.
SOURCE: CANCER RESEARCH, **(1995 Mar 1)** 55 (5) 1060-9.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 95171371
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950509
Last Updated on STN: 19950509

AB The pharmacokinetics, biodistribution, and dosimetry of an IgG1 radiolabeled anti-mucin mAb (**HMFG1**) and an isotype-matched control (4D513) were studied in 29 patients with primary head and neck squamous cell carcinoma. Patients were given injections at 3 fixed time points prior to surgery, i.e., 24 (n = 12), 48 (n = 9), or 72 (n = 8) h. They were subsequently classified into two groups based on their immunohistochemical positivity for **polymorphic epithelial mucin**. Fourteen patients (48%) were positive, 5 of which were studied with both antibodies; and 15 patients were negative (52%), 7 of which were studied with both antibodies. There was no significant difference in serum pharmacokinetics and cumulative urinary clearance of the two antibodies. There was no significant difference in overall normal tissue uptake of specific and control antibody; however, when each component of the normal tissue category was analyzed individually, there was a significantly increased uptake of **HMFG1** in mucosa as compared to control antibody. Immunohistochemical studies revealed positive staining of mucosa with **HMFG1**. There was significantly increased uptake of specific antibody in antigen-positive tumors as compared to uptake of control antibody ($P < 0.02$). A tendency for less label loss over time from positive tumors as compared to control was documented. Absolute antibody uptake and tumor/normal tissue ratios demonstrated significant overlap in individual patients from each category depending on the specific ratio (e.g., tumor/adipose tissue) or time point studied; hence arbitrary cutoff values could not be recommended as indicators of specific uptake. Specificity and localization indices were the most reproducible indicators of specific localization. Areas under the curve were calculated for all tissues, and local dosimetry for the two beta-emitting isotopes 131I and 90Y is presented. The Deq values for antigen-positive tumors were 2.9 cGy/mCi for 131I and 9.0 cGy/mCi injected for 90Y. For antigen-negative tumors these values were significantly lower at 0.83 and 2.4 cGy/mCi of 131I and 90Y, respectively. Bone marrow Deq was calculated to be 0.87 cGy/mCi of 131I-**HMFG1** injected. Because the purpose of our ongoing research is to assess the therapeutic potential of the combination of radiolabeled antibody and external radiotherapy, detailed dose calculation to local dose-limiting tissues is required. Deq to mucosa was calculated to be 1.1 and 3.8 cGy/mCi of injected 131I and 90Y, respectively. We conclude that a 9-10-Gy dose increment may be achieved in two administrations of 150 mCi of 131I-**HMFG1** during a course of external radiotherapy. This may lead to improved control of local disease in patients with head and neck cancer.

L13 ANSWER 40 OF 63 CANCERLIT on STN
ACCESSION NUMBER: 96053292 CANCERLIT
DOCUMENT NUMBER: 96053292 PubMed ID: 7584487
TITLE: The production and preclinical characterization of a **chimeric** anti-breast-cancer antibody, cBC2.
AUTHOR: Sutton V R; Burgess J; Pietersz G A; Li W J; McKenzie I F; Trapani J A
CORPORATE SOURCE: Austin Research Institute, Austin Hospital, Heidelberg, Victoria, Australia.
SOURCE: THERAPEUTIC IMMUNOLOGY, **(1994 Apr)** 1 (2) 83-93.
Journal code: 9421528. ISSN: 0967-0149.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 96053292
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960126
Last Updated on STN: 19970509

AB A **chimeric** (mouse-human) BC2 antibody (cBC2) was produced which may be used in the diagnosis and treatment of breast cancer. The BC2 variable region genes were amplified by polymerase chain reaction (PCR), using oligonucleotide primers homologous to the framework sequences of mouse VH and V kappa genes. The PCR products were used to create cBC2 expression vectors containing the mouse BC2 VH and V kappa and human constant region (IgG1 and K) genes. **Chimeric** antibody was produced following transfection of these constructs into Sp2/0 myeloma cells. Binding assays in vitro demonstrated that cBC2 had the same specificity for human **milk fat globule** membrane (**HMFGM**) and **MUC1**+ cells as mBC2, and bound antigen with a similar affinity (cBC2, Ka 5.53 +/- 2.09 x 10(8); mBC2, Ka 1.44 +/- 0.98 x 10(9)). Functionally, only cBC2 (5-25 micrograms ml-1), was able to mediate antibody-dependent cellular cytotoxicity (ADCC) with human effector cells, with 25% maximal specific lysis of **MUC1**+ cells at an E/T ratio of 100:1. Human complement-mediated lysis was minimal (10-15% specific lysis) with both mBC2 and cBC2. Neither cBC2 nor mBC2 was able to inhibit tumour growth in vivo in the absence of covalently coupled anticancer drugs. However, biodistribution studies demonstrated that both antibodies preferentially targeted **MUC1**+ tumour cells, with 17% of the injected dose of cBC2, as compared to 27% of mBC2, localized to the **MUC1**+ tumour at 24 h (less than 6% detected in any other tissue).

L13 ANSWER 33 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 91:644106 SCISEARCH
THE GENUINE ARTICLE: GQ744
TITLE: RECOGNITION OF PEPTIDYL EPITOPES BY **POLYMORPHIC EPITHELIAL MUCIN (PEM**)-SPECIFIC MONOCLONAL-ANTIBODIES
AUTHOR: DION A S (Reprint); SMORODINSKY N I; WILLIAMS C J; WRESCHNER D H; MAJOR P P; KEYDAR I
CORPORATE SOURCE: CTR MOLEC MED & IMMUNOL, INST MOLEC GENET, GARDEN STATE CANC CTR, 1 BRUCE ST, NEWARK, NJ, 07103 (Reprint); MCGILL UNIV, MCGILL CANC CTR, MONTREAL H3A 2T5, QUEBEC, CANADA; TEL AVIV UNIV, GEORGE S WISE FAC LIFE SCI, DEPT MICROBIOL, IL-69978 TEL AVIV, ISRAEL
COUNTRY OF AUTHOR: USA; CANADA; ISRAEL
SOURCE: HYBRIDOMA, (**1991**) Vol. 10, No. 5, pp. 595-610.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Peptidyl epitope recognition by several murine monoclonal antibodies (MAbs E29, H23, **HMFG**-1, **HMFG**-2, MA5, MA6 and MA9) which react with the **polymorphic epithelial mucins** [**PEM**; epithelial membrane antigen (EMA)] was studied by using ten synthetic peptides representative of the 20 residue tandem repeat as test antigens. Antibody binding to 6-10 residue overlaps and to peptides having a common carboxy-terminus and staggered amino-termini (8-31 residues) was assessed by solid phase and competition ELISA techniques. From these analyses, all MAbs except MA9 were found to react predominantly with the carboxy-terminal half of the repeat motif. Polyclonal antibody responses in mice immunized with intact EMA/**PEM**-containing preparations also displayed significant reactivities against synthetic repeat peptide antigens and, conversely, synthetic peptides as carrier-**conjugated** immunogens induced antibodies recognizing intact antigens. These results are discussed vis-a-vis peptide conformation, the potential effects of O-glycosylation on secondary structure, and the possible effects of these parameters on immunogenicity and antigenicity.

L13 ANSWER 29 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 95:180217 SCISEARCH
THE GENUINE ARTICLE: QK187
TITLE: CELLULAR MUCINS - TARGETS FOR IMMUNOTHERAPY
AUTHOR: APOSTOLOPOULOS V; MCKENZIE I F C (Reprint)
CORPORATE SOURCE: AUSTIN RES INST, STUDLEY RD, HEIDELBERG, VIC 3084, AUSTRALIA (Reprint); AUSTIN RES INST, HEIDELBERG, VIC 3084, AUSTRALIA
COUNTRY OF AUTHOR: AUSTRALIA
SOURCE: CRITICAL REVIEWS IN IMMUNOLOGY, (**1994**) Vol. 14, No. 3-4, pp. 293-309.
ISSN: 1040-8401.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 82

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Mucins are attracting great interest as potential targets for immunotherapy in the development of vaccines for cancers expressing Mucin1 (**MUC1**) (e.g., breast, pancreas, ovary, and others) as there is (1) a 10-fold increase in the amount in adenocarcinomas; (2) an alteration in expression where they become ubiquitous, acid (3) due to altered glycosylation, new epitopes appear on the cell surface that are absent in normal tissues. These new epitopes can be carbohydrate; others are peptide in nature. The cloning of the cDNAs from mucins, particularly **MUC1** , has led to rapid advances being made, and it is clear that a highly immunogenic peptide exists within the variable number of tandem repeats (VNTR) found in all mucins. This peptide is immunogenic in mice, giving rise to strong antibody production, and most monoclonal antibodies made to breast cancer, which react with the protein core, react with the peptide APDTR. It is now also clear that humans with breast cancer have, in their draining lymph nodes, precursors of cytotoxic T cells that can be stimulated in vitro to react against breast cancer and indeed against the APDTR or a closely related peptide - shown from antibody-blocking studies. These CTLs are unique in that they are non-MHC restricted. The identification of suitable targets, coupled with the known immunogenicity of both the peptide and neo-carbohydrate epitopes, has led to the development of several different programs to immunize humans against breast cancer using either synthetic carbohydrates or peptides **conjugated** with adjuvants, and clinical trials are now in progress to evaluate their immunogenicity and anti-cancer effects.

L13 ANSWER 12 OF 63 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:244989 BIOSIS
DOCUMENT NUMBER: PREV200000244989
TITLE: A DNase I based **immunotoxin** for tumor therapy.
AUTHOR(S): Young, Robert J. (1); Verma, Rakesh; Dhokia, Babu S.; Cook, Julie A.; Deonarain, Mahendra P.; Rowlinson-Busza, Gail; Courtenay-Luck, Nigel S.; Epenetos, Agamenon A.
CORPORATE SOURCE: (1) Antisoma Research Laboratories, London UK
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (**March, 2000**) No. 41, pp. 289.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L23 ANSWER 12 OF 14 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 86266972 MEDLINE
DOCUMENT NUMBER: 86266972 PubMed ID: 3460375
TITLE: An antibody-toxin conjugate directed against a human mammary cancer antigen.
AUTHOR: Monaco M E; Mack J; Dugan M D; Ceriani R
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, **(1986)** 464 389-99.
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198608
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860812

AB A conjugate has been constructed consisting of diphtheria toxin fragment A (DTA) linked to a monoclonal antibody, BLMRL-**HMFG**-Mc5 (MC5), directed against a mammary cancer antigen. The conjugate retains both binding and DTA enzymatic activity when tested against target MCF-7 cells, although the conjugate binds less well than the unconjugated antibody. The conjugate is toxic to MCF-7 cells. Toxicity is both dose- and time-dependent. Half-maximal toxicity is observed with 2-5 X 10(-8) M conjugate after 5 days of incubation. However, the conjugate need only be in contact with the cells for 1 day in order to effect complete killing by 5 days. The earliest that an effect can be seen on cell growth is 2 days. When tested against WRK-1 rat mammary tumor cells, the conjugate is inactive.

L23 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:623061 CAPLUS
DOCUMENT NUMBER: 127:283398
TITLE: Method of killing target cells in harvested cell populations with one or more immunotoxins
INVENTOR(S): Fodstad, Oystein; Kvalheim, Gunnar; Juell, Siri; Wang, Meng Yu; Engebraten, Olav
PATENT ASSIGNEE(S): Fodstad, Oystein, Norway; Kvalheim, Gunnar; Juell, Siri; Wang, Meng Yu; Engebraten, Olav
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9733611	A1	19970918	WO 1997-NO74	19970312	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2248620	AA	19970918	CA 1997-2248620	19970312	<--
AU 9725229	A1	19971001	AU 1997-25229	19970312	<--
AU 710184	B2	19990916			
CN 1218411	A	19990602	CN 1997-194599	19970312	<--
BR 9708049	A	19990727	BR 1997-8049	19970312	<--
EP 954329	A1	19991110	EP 1997-916665	19970312	<--
EP 954329	B1	20020814			
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NZ 331763	A	20000128	NZ 1997-331763	19970312	<--
JP 2000507230	T2	20000613	JP 1997-532482	19970312	<--
RU 2182493	C2	20020520	RU 1998-118574	19970312	
AT 222122	E	20020815	AT 1997-916665	19970312	
NO 9804175	A	19980910	NO 1998-4175	19980910	<--
US 2002151689	A1	20021017	US 1998-125751	19981030	
NZ 336576	A	20000825	NZ 1999-336576	19990705	<--

PRIORITY APPLN. INFO.:

NO 1996-1031	A	19960313
NZ 1997-331763	A1	19970312
WO 1997-NO74	W	19970312

AB Unwanted malignant target cells in a cell population are killed by exposing the cell population in vitro or in vivo to a synergistic combination of .gtoreq.2 immunotoxins which selectively kill malignant cells. The cell population comprises an autologous stem cell transplant of nucleated cells harvested from peripheral blood of cancer patients, or CD34+ or similar early progenitor cells selected from these nucleated cells or from bone marrow aspirates. The immunotoxins comprise .gtoreq.2 antibodies conjugated with bacterial toxins, the antibodies being directed to target cell-assocd. antigens, and are not toxic to normal progenitor cells. Thus, antibodies to **MUC1** (a mucin antigen found mainly on breast cancer cells) and to EGP2 (another breast cancer cell antigen) were both conjugated with Pseudomonas exotoxin A via a thioether bond formed with sulfosuccinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate. A mixt. of these antibody-toxin conjugates was incubated with PM1 human breast cancer cells in the presence of CD34+ peripheral blood stem cells (mobilized in non-Hodgkin lymphoma patients by pretreatment with chemotherapy and G-CSF). All clonogenic tumor cells

were killed within 60 min.

L13 ANSWER 46 OF 63 CANCERLIT on STN
ACCESSION NUMBER: 91668421 CANCERLIT
DOCUMENT NUMBER: 91668421
TITLE: BREAST CANCER IMMUNODIAGNOSIS AND IMMUNOTHERAPY.
AUTHOR: Anonymous
CORPORATE SOURCE: No affiliation given.
SOURCE: Non-serial, **(1989)** Breast Cancer Immunodiagnosis and Immunotherapy. Ceriani RL, ed. New York, Plenum, 259 p., 1989. .
DOCUMENT TYPE: Book; (MONOGRAPH)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19941107
Last Updated on STN: 19941107

AB After almost a decade of research in the basic and applied aspects of the use of serologic means to diagnose and possibly treat breast cancer, several milestones have been reached. These include a clear understanding of the immunopathologic use and limitations of monoclonal antibodies (MoAbs) against breast epithelium, the development and clinical use of immunoassays for circulating breast epithelial antigens, advances in the diagnostic use of MoAbs to estrogen and progesterone receptor proteins, and the first communications on proposed therapeutic use of different **conjugates** of antibreast antibodies. This volume contains contributions to the Third International Workshop on Monoclonal Antibodies and Breast Cancer, held in San Francisco, California, on November 17-18, 1988. Topics include synthetic tumor-associated glycoconjugates for generating MoAbs for breast cancer imaging and specific immunotherapy, extracellular keratins, MoAbs Mc5 and BrE1, MoAbs for identifying and isolating breast tumor-associated antigens, DF3 breast cancer-associated antigen, an assay for cryptic tumor antigens, biosynthesis of cell surface sialomucin, core protein epitopes of a **polymorphic epithelial mucin**, cell heterogeneity and complexity of breast epithelial surface antigens, oncogenic potential of membrane receptor proteins encoded by human erbB proto-oncogenes, estrogen and progesterone receptors, MoAbs against steroid receptors and steroid-induced proteins, 10-yr survival patterns in primary breast cancers (hormone receptor antigen detection by MoAbs) steroid receptor immunoassay, H23 MoAbs recognizing breast tumor-associated antigen, complementation of MoAbs DF3 and B72.3 in reactivity to breast cancer, differential expression of DF3 antigen between papillary carcinomas and benign papillary breast lesions, potentiation of antitumor activity by combined administration of interferon alpha and an antibreast epithelial MoAb, immunolymphoscintigraphy with BCD-F9 MoAb and its F(ab')2 fragments for the preoperative staging of breast cancers, reaction of antibodies to human **milk fat globule** with synthetic peptides, drug immunoconjugates in cancer treatment, a Phase I study of antibreast cancer **immunotoxin** 2609 MoAb-rRA given by continuous infusion, and in vivo studies of radiolabeled MoAbs MC5 and KC4.

L13 ANSWER 48 OF 63 LIFESCI COPYRIGHT 2003 CSA on STN
ACCESSION NUMBER: 95:103126 LIFESCI
TITLE: The production and preclinical characterization of a **chimeric** anti-breast-cancer antibody, cBC2
AUTHOR: Sutton, V.R.; Burgess, J.; Pietersz, G.A.; Li, W.J.; McKenzie, I.F.C.; Trapani, J.A.
CORPORATE SOURCE: Austin Res. Inst., Austin Hosp., Studley Rd., Heidelberg, Vic. 3084, Australia
SOURCE: THER. IMMUNOL., (**1994**) vol. 1, no. 2, pp. 83-93. ISSN: 0967-0149.
DOCUMENT TYPE: Journal
FILE SEGMENT: F; W3
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A **chimeric** (mouse-human) BC2 antibody (cBC2) was produced which may be used in the diagnosis and treatment of breast cancer. The BC2 variable region genes were amplified by polymerase chain reaction (PCR), using oligonucleotide primers homologous to the framework sequences of mouse V sub(H) and V Kappa genes. The PCR products were used to create cBC2 expression vectors containing the mouse BC2 V sub(H) and V Kappa and human constant region (IgG1 and K) genes. **Chimeric** antibody was produced following transfection of these constructs into Sp2/0 myeloma cells. Binding assays in vitro demonstrated that cBC2 had the same specificity for human **milk fat globule** membrane (**HMFGM**) and **MUC1** super(+) cells as mBC2, and bound antigen with a similar affinity (cBC2, Ka 5.53 plus or minus 2.09 x 10 super(8); mBC2, Ka 1.44 plus or minus 0.98 x 10 super(9)). Functionally, only cBC2 (5-25 mu g/ml), was able to mediate antibody-dependent cellular cytotoxicity (ADCC) with human effector cells, with 25% maximal specific lysis of **MUC1** super(+) cells at an E/T ratio of 100:1. Human complement-mediated lysis was minimal (10-15% specific lysis) with both mBC2 and cBC2. Neither cBC2 nor mBC2 was able to inhibit tumour growth in vivo in the absence of covalently coupled anticancer drugs. However, biodistribution studies demonstrated that both antibodies preferentially targeted **MUC1** super(+) tumour cells, with 17% of the injected dose of cBC2, as compared to 27% of mBC2, localized to the **MUC1** super(+) tumour at 24 h (less than 6% detected in any other tissue).

L13 ANSWER 50 OF 63 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1996-02720 BIOTECHDS
TITLE: Generation of murine monoclonal antihuman **milk fat globule** membrane antibodies using immunoprecipitation and BIAcore analyses; lipid monoclonal antibody production from a hybridoma cell culture, for application as a diagnostic, and in mamma carcinoma therapy
AUTHOR: Bynum J; Hutchins J T; *Kull Jr F C
CORPORATE SOURCE: Glaxo-Wellcome
LOCATION: Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709, USA.
SOURCE: Hybridoma; (**1995**) 14, 6, 587-91
CODEN: HYBRDY
ISSN: 0272-457X
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1996-02720 BIOTECHDS
AB A selection of monoclonal antibodies (MAbs) was developed against deoxycholine-solubilized human **milk fat globule** membranes (**HMFG**). Groups of BALB/c mice and SJL/J mice were immunized with each of the **HMFG** pools i.d. in multiple sites. The mice were boosted twice at monthly intervals. Mice were test bled prior to cell **fusion**. 4 Days before **fusion**, selected mice were boosted i.p. or i.v. with 200 ug of **HMFG** in normal saline. P3X63-Ag8.653 cell **fusions** were performed using PEG-1500 and the **fusion** mixtures were plated. Wells of interest were expanded and then cloned. The MABs were selected for their ability to immunoprecipitate 125I-labeled **HMFG** and then further analyzed by surface plasmon resonance on the BIAcore for their reactivity with **HMFG** and with a **fusion** protein containing a 4 mer of the **muc**-1 tandem repeat. 4 Of the 6 MAbs appeared to react more intensely with tumor compared to normal mamma tissues. One of those MAbs reacted with the **fusion** protein 4-mer of the **muc**-1 tandem repeat. These MAbs may be used potentially as diagnostics or in therapy. (20 ref)